

Hyperfractionated radiotherapy and cetuximab with concurrent chemotherapy in locally advanced stage IV head and neck carcinomas



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Introduction. Treatment of locally advanced squamous cell carcinomas of head and neck (LA-SCCHN) is evolving. The aim of the present study is to analyze clinical outcomes and toxicity in far advanced cancer with combined triple therapy of chemotherapy (CHT), hyperfractionated radiotherapy (HF-RT) and cetuximab (CTX).

Material and methods. 27 newly diagnosed LA-SCCHN patients were included between September 2009 and December 2012. RT consisted in HF-RT: 1.15 Gy/fraction, BID, 5 days/week, 7 weeks. Carboplatin was administered 5 mg/m² before each fraction of RT. Cetuximab was administered 400 mg/m² one week before RT-CTH and then 250 mg/m² weekly while RT-CHT. Patients were evaluated for response two months after completing treatment. Toxicity was scored by CTCA 4.0 criteria.

Results. Median age was 51.6 years (44–65), 85% were males. All patients were stage IV. Tumors were located mainly in oropharynx (47%) and hypopharynx (30%). One patient were excluded due to an allergic reaction in the first infusion of CTX and 26 patients (96%) received the complete planned treatment and were evaluated for response. All patients achieved objective response, 22 (85%) had a complete response (CR) and 4 a partial response. Two patients with CR had a locoregional relapse (one with synchronous pulmonary metastasis). 3 out of 6 patients with progressive disease were eligible either for surgical rescue (1) or CHT (2). With a median follow-up of 16.7 months (5–39), 23 of 26 patients were alive, with an actuarial survival at 3 years of 88.5%. Massive nodal invasion N3 was a strong prognostic factor for survival ($p < 0.007$). Among the 26 evaluable patients for toxicity, 85% had grade 3 radiodermatitis and 82% grade 3 mucositis. Acneiform rash was grade 3 in 78% of the patients.

Conclusion. This is a feasible treatment in patients with an optimal Karnofsky Status and far advanced SSCCHN obtaining an immediate response in all cases, with an acceptable tolerance and encouraging overall survival figures.

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Hypopharyngeal cancer and organ preservation



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Introduction. Hypopharyngeal cancer accounts for about a quarter of all malignancies of the head and neck. The diagnosis in advanced stages and high incidence of early metastases, place overall survival rates after five years on figures from 30% to 35%. No treatment by itself, surgery at different options, radiotherapy and/or chemotherapy, offers a clear advantage in survival.

Purpose. A descriptive study of 83 patients with hypopharyngeal cancer treated with radiotherapy (initial stage) or concomitant radiotherapy and chemotherapy (neoadjuvant chemotherapy and radio-chemotherapy, or radiotherapy and concurrent chemotherapy) as a first therapeutic option in the period from January 2008 to June 2012.

Methods. 68% of patients were smokers and 76.5% alcohol at the time of diagnosis. The symptom of initial consultation was the presence of a lateral adenopathy. In 75% of patients followed by odynophagia. With regard to staging the initial stages were 2.6% and 97% advanced stage with 78% stage IV. In 7.7% had local or locoregional surgical salvage for persistent or recurrent tumor.

Results. Of all patients 64% died of distant metastases or locoregional relapse. Increased risk of locoregional recurrence or distant metastasis is located in the first two years, in the first year was detected in 63% of patients and the second years was detected in 37% of patients.

Conclusions. The improvement in overall survival in carcinoma of the hypopharynx is still present a challenge for professionals. The initial therapeutic option will depend on the patient, tumor stage, status performance, the experience of professionals and treatment facilities available. Treatment decisions should be decided by a Committee Head and Neck Cancer and multidisciplinary therapy that will be essential in the comprehensive management of the tumor.

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IMRT in nasopharyngeal cancer patients with skull base infiltration



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Radiotherapy, with or without chemotherapy, is the standard treatment of nasopharyngeal cancer. IMRT allows to give higher dose to the PTV, and lower dose to adjacent organs. We reviewed our experience with this group of patients. We wished to assess the local control (partial or total response on CT or MRI evaluation) and incidence of late side-effects incidence. Between February 2007 and March 2012, we treated 16 nasopharyngeal cancer patients with skull base infiltration (T4 stage) with IMRT. Eleven were males and five females, median age 65 (range 15–81). Thirteen patients had undifferentiated carcinoma (81%) and 3 squamous carcinoma (19%). Six patients were treated with forward IMRT: 72–74 Gy of total dose, 1.8 Gy per day, 40 days. Remaining 10 patients (62%) were treated with inverse planification IMRT: 70–73 Gy ($m = 72$) 2.20–2.35 Gy/fraction ($m = 2.29$) 30–32 fractions ($m = 30.2$). Six patients received neoadjuvant chemotherapy (37%), and 14 concomitant and adjuvant chemotherapy (87%) Median follow-up is

4.3 years (3 month–6 years). One patient died three months after the end of the treatment due to the tumor spread in CSF. We observe local control at 1-year follow-up in 13 of the remaining patients (81%). Two patients relapsed in the cavernous sinus and in Eustachian tube/middle ear respectively. Both patients were subsequently treated with reirradiation using IMRT achieving a complete response that persists nowadays. Two patients (12%) died from lung metastasis without evidence of local relapse. Side-effects: nasal dryness 60%, G1 and G2 xerostomia (33% and 7% of patients respectively), otitis media in 40%, esophageal stenosis 7%. One of three patients with pericarotid tumor involvement developed massive hemorrhage due to the rupture of a carotid aneurysm that required urgent vascular surgery. IMRT was associated with excellent local control and survival. Inclusion of more patients and a longer follow-up are required to confirm these results

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Induction chemotherapy with docetaxel, cisplatin and 5-fluorouracil (TPF) followed by radiation and concurrent cetuximab or cisplatin in locally advanced squamous cell carcinoma of the head and neck



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Background. We conducted a prospective study in patients with locoregionally advanced head and neck squamous cell cancer (LAHNC) to evaluate the feasibility and efficacy of combining 3-drug taxane-containing induction chemotherapy (IC) with radiation and concomitant single-agent cetuximab or cisplatin.

Methods. Three cycles of TPF induction chemotherapy with prophylactic G-CSF followed by definitive radiation and concurrent cetuximab (400 mg/m² loading dose and 250 mg/m² per week during RT) or cisplatin (30 mg/m²/w or 100 mg/m² 120-h continuous infusion of weeks 1 and 5). Radiotherapy was delivered with accelerated hyperfractionation concomitant boost (72 Gy/42 fr/6 w) or standard fractionation (70 Gy/35 fr/7 w).

Results. There were 51 eligible and evaluable patients enrolled between May 1, 2007, and August 31, 2012. According to the AJCC 6 ed., 2010, 48 (94%) had stage IV disease and 3 (5.9%) stage III. Larynx 24 (45.5%) was the most common site followed by oropharynx 10 (19.6%), hypopharynx 10 (19.6%), oral cavity 3 (5.9%), nasopharynx 2 (3.9%) and paranasal sinus 1 (1.9%). Concurrent with radiotherapy 42 patients (82.3%) received cetuximab and 9 patients (17.6%) cisplatin. The percentage of patients completing ICT was 98.04%, radiation 100%, and cetuximab or cisplatin 98%. During TPF G 3 non-haematological toxicity occurred in 7 patients (13.7%) and G4 in 2 (3.9%). Acute G 3–4 toxicity of concurrent treatment included dermatitis in 37 patients (36 G3, 1 G4) and mucositis in 39 (38 G3, 1 G4). Forty-five percent of patients received enteral feeding. The overall response rate was 94.1%. Tumor response (RECIST) at 12 weeks following completion treatment was 64.7% complete response and 29.4% partial response. The 2.5-year overall survival estimates were 58.1%, with 2.5-year progression-free survival estimates of 55.3% and 2-year local control estimates of 81.3%.

Conclusions. Triple drug-based sequential therapy in patients with LAHNC is tolerable, with encouraging efficacy.

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Institutional experience for replanning in head and neck tumor IMRT



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Purpose. Is described our experience in protocol for adaptive radiotherapy for head and neck tumors treated with Boost integrated IMRT.

Material and method. IMRT in head and neck cancer provides an essential role in such diseases, and this technique provides a high level of coverage with a low threshold dose distribution in critical organs (cord, brainstem, mandible, parotid glands), comparing to 3D conventional technique. (a) Starting from 2011 we began conducting the protocol to assess replanning in IMRT: a new CT-scan is performed at 4 weeks from starting treatment and is fused with the preplanning-CT as a dose of 45 Gy; when there nodal regression and inclusion of the parotids to the high dose region, and for that dose, weight loss is more apparent on the anatomical structures of the head and neck. (b) 79 patients were treated between 2011 and 2012 with the diagnosis head and neck cancer. We report our experience for replanning in IMRT treatment. (c) 14 of 79 patients (17%) were replanificated with